REMARKS

The Applicant expresses appreciation to the Examiner for consideration of the subject patent application. This amendment is in response to the Office Action mailed March 26, 2004. The disclosure was objected to. Claims 1-15 were rejected. The claims and specification have been amended to address the concerns raised by the Examiner. The specification is revised in order to correct grammatical, idiomatic and spelling informalities and to more specifically describe the invented subject matter. Support for the amendments can be found throughout the specification and no new matter has been added into the amendments.

Claims 1-15 were originally presented. Claims 1-15 have been canceled without prejudice. Claims 16-22 have been added.

Claim Rejections - 35 U.S.C. § 112

The specification is objected to and Claims 1-14 stand rejected under §112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure. Specifically, the specification does not provide evidence that the claimed biological materials are deposited in compliance with the criteria set forth in 37 CFR section 1.801-1.809. It is respectfully submitted that the deposits of hybridomas R813 and Y262 under the terms of the Budapest Treaty were made with the China General Microbiological Culture Collection Center(CGMCC) on July 14, 2003. The information regarding the deposits is added to the amended specification and a declaration by the Applicant regarding the depository is also enclosed. Therefore, the Examiner is respectfully requested to withdraw the rejection under §112, first paragraph.

Claims 1-4 and 10-12 stand rejected under § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-14 stand rejected under § 112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is respectfully submitted that the new claims are drafted in order to overcome the 112 rejections of the old claims and no new matter is added in the new claims.

Claim Rejections - 35 U.S.C. § 102

Claims 10 and 15 were rejected under 35 U.S.C. § 102(b) as being anticipated by Coller et al. (US Pat. No. 5,387,413, hereafter referred as "'413"). Claim 10 was rejected under 35 U.S.C. § 102(b) as being anticipated by Coller et al. (US Pat. No. 5,770,198, hereafter referred as "'198"). Claims 10 was rejected under 35 U.S.C. § 102(b) as being anticipated by Co et al.(US Pat. No. 5,387,413, hereafter referred as "'413"). In order to most succinctly explain why the claims presented herein are allowable, Applicant will direct the following remarks primarily to the new independent claim 16 with the understanding that once an independent claim is allowable, all claims depending therefrom are allowable.

All references cited fail to disclose a combination of the whole or a fragment of the monoclonal antibody R813 obtained from hybridoma CGMCC No. 0740 which specifically recognizes GPIIIa and the whole or a fragment of the monoclonal antibody Y262 obtained from hybridoma CGMCC No. 0741 which specifically recognizes GPIIb-IIIa complexes.

The new claims are directed to a pharmaceutical composition capable of efficiently inhibiting platelet aggregation, comprising two monoclonal antibodies, R813 and Y262 together. However, neither of the references cited by the Examiner disclose such a combination of the two monoclonal antibodies. Therefore, none of the current claims is anticipated by the references cited.

The elements of a "cock tail" combination of the two monoclonal antibodies are not taught in any of the cited references and provides the advantage of better performance because the "cocktail" composition of the two monoclonal antibodies not only decreases the dose of monoclonal antibody substantially but also greatly increases inhibition of platelet aggregation. The experimental results indicate that R813 and Y262 act on different sites of the platelet GPIIb-IIIa complex and the "cocktail" of these two antibodies completely blocks the binding of fibrinogen to the platelet GPIIb-IIIa receptor and thus inhibits platelet aggregation. Additionally, the $F(ab')_2$ fragments of these two monoclonal antibodies still completely inhibit platelet aggregation, the biological activities of which exceed that of 7E3 as disclosed in the references.

Therefore, the Applicant respectfully submits that claims 16-22 are not anticipated by any of the cited references, and urges the Examiner to withdraw the rejection.

Claim Rejections - 35 U.S.C. § 103

Claims 2, 4, 6, 7, 9and 12 were rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as being unpatentable over Coller et al. (US Pat. No. 5,387,413, hereafter referred as "'413") or Coller et al. (US Pat. No. 5,770,198, hereafter referred as "'198") Claims 1, 3, 5, 7, 8 and 11 were rejected under 35 U.S.C. § 103(a) as being unpatentable over '198 in view of '413.

In order to most succinctly explain why the claims presented herein are allowable, the Applicant will direct the following remarks primarily to the amended independent claim 1 with the understanding that once an independent claim is allowable, all claims depending therefrom are allowable.

The applicant respectfully submits that the presently amended claims are not obvious in view of the reference cited. In other words, one of ordinary skill in the art, when combining all teachings of the reference of record at the time the invention was made, would not have been motivated to come up with the presently claimed invention.

The initial burden is on the Examiner to establish a case of *prima facie* obviousness. The test for establishing such a case is well stated in *In re Vaeck*, 947 F.2d 488, 20USPQ2d 1438 (Fed. Cir.1991) as follows:

> "To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and reasonable expectation of success must both be found in the prior art, and not based on the applicant's disclosure."

When applying 35 U.S.C. 103, the following tenets of patent law must be

adhered to: (A) The claimed invention must be considered as a whole; (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (c) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and (D) reasonable expectation of success is the standard with which obviousness is determined. Hodosh v. Block Drug Co., Inc., 786 F.2d 1136, 1143 n.5, 229 USPQ 182,187 n.5 (Fed. Cir. 1986)

Under this statement of law, the Applicants respectfully submit that the present invention would not be obvious over '198 in view of '413. Both '198 and '413 are directed to a sole monoclonal antibody specific for the GPIIb/IIIa complex and no combination of different monoclonal antibodies was disclosed or suggested in either of the references. To the contrary, in the current claims of the instant application, a combination of two different monoclonal antibodies is disclosed for completely inhibiting platelet aggregation. The essence of the present invention lies in the combination of monoclonal antibody R813, which specifically acts on platelet GPIIIa, and monoclonal antibody Y262, which specifically acts on platelet GPIIb-IIIa complexes.

As indicated in the specification, the drawback of monoclonal antibody 7E3 disclosed in the cited references is that it only act on one epitope on the platelets and blocks the function of the receptor in a single way and thus cannot achieve complete inhibition of platelet aggregation. It is respectfully submitted that the composition of the present invention is substantially different from the cited references because the combination of the two monoclonal antibodies as claimed in the present invention acts on two different epitopes of the platelet GP IIb-IIIa complex and is capable of completely blocking the function of the platelet GP IIb-IIIa complex receptor and inhibiting platelet aggregation. From the experimental data as disclosed in Example 5, it is obvious that combined use of R813 and Y262 exhibits enhanced inhibition and anti-thrombotic activity which is superior to that of 7E3 (cf. Tables 2, 3 and 4).

It is respectfully submitted that the '413 and '198 references, when combined, do not teach or suggest all of the elements of the new claim16. Specifically, neither of the cited references teach a combination of two monoclonal antibodies which act on two different epitopes of the platelet GP IIb-IIIa complex , and the combination of the cited references does not overcome that

deficiency.

That is to say, the combination of monoclonal antibodies R813 and Y262 is definitely not obvious to a person skilled in the art, and the enhanced activity of inhibition of the present composition would in no way be expected by a person skilled in the art. Therefore, the claimed invention is not obvious in view of the references cited by the Examiner, and the rejection under 35 U.S.C. section 103 is respectively requested to be withdrawn.

The Office Action has asserted that it would be obvious to one of skill in the art to come up with the present invention, but has cited no basis for that assertion. Therefore, it is respectfully submitted that the Examiner has failed to establish a case of *prima facie* obviousness because: first, there is no suggestion or motivation to modify the reference or to combine reference teachings; second, there is no reasonable expectation of success and finally, the prior art references, even when combined, still fail to teach or suggest all the limitations as claimed in the present invention. Therefore, the Applicant respectfully submits that Claims 16-22 (including independent claim 16) are allowable, and urges the Examiner to withdraw the rejection.

CONCLUSION

In light of the above, the Applicant respectfully submits that pending claims 16-22 are now in condition for allowance. Therefore, the Applicant requests that the rejections and objections be withdrawn, and that the claims be allowed and passed to issue. If any impediment to the allowance of these claims remains after entry of this Amendment, the Examiner is strongly encouraged to call Weili Cheng Ph.D, or in her absence, the undersigned at (801) 566-6633 so that such matters may be resolved as expeditiously as possible.

Check No. 20294, in the amount of $475.00, is enclosed pursuant to 37 C.F.R. § 1.17(a)(3), for a three month extension of time pursuant to 37 C.F.R. § 1.136. 7 claims were added (claims 16-22), including 1 independent claim (claim 16), while 15 claims were canceled (claims 1-15), including 6 independent claims (claims 1, 2, 7, 10, 13 and 15). Therefore, no additional fee is due.

The Commissioner is hereby authorized to charge any additional fee or to credit any overpayment in connection with this Amendment to Deposit Account No. 20-0100.

DATED this 20th day of September, 2004.

Respectfully submitted,

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